

What is claimed is:

1. An isolated composition comprising a conformational epitope of a protofibrillar aggregate which a) forms in a human or animal and b) contributes to amyloid fibril formation.
- 5 2. A composition according to claim 1 wherein the composition is synthetic.
3. A composition according to claim 1 wherein the composition
10 comprises a peptide.
4. A composition according to claim 3 wherein the peptide is conformationally constrained.
- 15 5. A composition according to claim 3 wherein the peptide is selected from the group consisting of SEQ ID NO. 1, SEQ ID NO. 2, SEQ ID NO. 3, SEQ ID NO. 4, SEQ ID NO. 5, SEQ ID NO. 6, SEQ ID NO. 7, SEQ ID NO. 8, SEQ ID NO. 9 and mixtures thereof.
- 20 6. A composition according to claim 3 wherein the peptide is SEQ ID NO. 1.
7. A composition according to claim 1 wherein the composition is supported by a surface.
- 25 8. A composition according to claim 7 wherein the surface is curved or flat.
9. A composition according to claim 7 wherein the surface comprises
30 solid matter.
10. A composition according to claim 7 wherein the surface comprises a surface of a film or a particle or a sheet.
- 35 11. A composition according to claim 7 wherein the surface comprises a protein.

12. A composition according to claim 11 wherein the protein comprises a α -pleated sheet.

13. A composition according to claim 7 wherein the composition is bound to the support surface.

14. A composition according to claim 7 wherein the composition is chemically bonded to the support surface.

15. A composition according to claim 14 wherein the chemical bond is a covalent bond.

16. A composition according to claim 7 wherein the support comprises a material selected from the group consisting of gold, zinc, cadmium, tin, titanium, silver, selenium, gallium, indium, arsenic, silicon, mixtures thereof and combinations thereof.

17. A composition according to claim 1 wherein the protofibrillar aggregate has a molecular weight in a range of about 1 kDa to about 100,000,000 kDa.

18. A composition according to claim 1 wherein the protofibrillar aggregate comprises five or more monomers.

19. A composition according to claim 1 wherein the protofibrillar aggregate comprises eight monomers.

20. A composition according to claim 1 wherein amyloid peptide monomers are substantially free of the epitope.

21. A composition according to claim 1 wherein amyloid fibrils are substantially free of the epitope.

22. A composition according to claim 1 wherein the protofibrillar aggregate comprises a toxic species.

23. A composition according to claim 1 wherein the protofibrillar aggregate is present in a human or animal having a disease characterized by amyloid deposits.

5 24. A composition according to claim 23 wherein the disease is selected from the group consisting of Alzheimer's, early onset Alzheimer's associated with Down's syndrome, SAA amyloidosis, hereditary Icelandic syndrome, multiple myeloma, and spongiform encephalopathies, including mad cow disease, sheep scrapie, and mink spongiform encephalopathy, Parkinson's disease, Huntington's
10 disease, amyotrophic lateral sclerosis, Creutzfeldt Jakob disease, Gerstmann-Straussler-Scheinker syndrome, kuru, fatal familial insomnia, chronic wasting syndrome, familial amyloid polyneuropathy, frontotemporal dementia, type II diabetes, systemic amyloidosis, serum amyloidosis, British familial dementia, Danish familial dementia, macular degeneration and cerebrovascular amyloidosis.

15 25. A composition according to claim 23 wherein the disease is Alzheimer's.

20 26. The synthetic composition of claim 1 wherein the composition is a pharmaceutical composition.

27. A composition according to claim 1 wherein the composition is a vaccine.

25 28. An isolated composition comprising an epitope of a protofibrillar aggregate which forms in a human or animal contributing to an amyloid fibril formation wherein the amyloid fibril is substantially free of the epitope.

30 29. A composition according to claim 28 wherein the composition is synthetic.

30. A composition according to claim 28 wherein amyloid peptide monomers are substantially free of the epitope.

35 31. A composition according to claim 28 comprising a peptide.

32. A composition according to claim 31 wherein the peptide is conformationally constrained.

5 33. A composition according to claim 31 wherein the peptide is selected from the group consisting of SEQ ID NO. 1, SEQ ID NO. 2, SEQ ID NO. 3, SEQ ID NO. 4, SEQ ID NO. 5, SEQ ID NO. 6, SEQ ID NO. 7, SEQ ID NO. 8, SEQ ID NO. 9 and mixtures thereof.

10 34. A composition according to claim 31 wherein the peptide is SEQ ID NO. 1.

35. A composition according to claim 28 wherein the composition is supported by a surface.

15 36. A composition according to claim 35 wherein the surface is curved or flat.

20 37. A composition according to claim 35 wherein the surface comprises solid matter.

38. A composition according to claim 35 wherein the surface is a film or a particle or a sheet.

25 39. A composition according to claim 35 wherein the surface comprises a protein.

40. A composition according to claim 39 wherein the protein comprises a α -pleated sheet.

30 41. A composition according to claim 35 wherein the composition is bound to the support surface.

35 42. A composition according to claim 35 wherein the composition is chemically bonded to the support surface.

43. A composition according to claim 42 wherein the chemical bond is a covalent bond.

44. A composition according to claim 35 wherein the support comprises a material selected from the group consisting of gold, zinc, cadmium, tin, titanium, silver, selenium, gallium, indium, arsenic, silicon, mixtures thereof and combinations thereof.

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45. A composition according to claim 28 wherein the protofibrillar aggregate has a molecular weight in a range of about 1 kDa to about 100,000,000 kDa.

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46. A composition according to claim 28 wherein the protofibrillar aggregate comprises five monomers.

47. A composition according to claim 28 wherein the protofibrillar aggregate comprises eight monomers.

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48. A composition according to claim 28 wherein the protofibrillar aggregate comprises a toxic species.

49. A composition according to claim 28 wherein the protofibrillar aggregate is present in a human or animal having a disease characterized by amyloid deposits.

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50. A composition according to claim 49 wherein the disease is selected from the group consisting of Alzheimer's, early onset Alzheimer's associated with Down's syndrome, SAA amyloidosis, hereditary Icelandic syndrome, multiple myeloma, and spongiform encephalopathies, including mad cow disease, sheep scrapie, and mink spongiform encephalopathy, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, Creutzfeldt Jakob disease, Gerstmann-Straussler-Scheinker syndrome, kuru, fatal familial insomnia, chronic wasting syndrome, familial amyloid polyneuropathy, frontotemporal dementia, type II diabetes, systemic amyloidosis, serum amyloidosis, British familial dementia, Danish familial dementia, macular degeneration and cerebrovascular amyloidosis.

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51. A composition according to claim 49 wherein the disease is Alzheimer's.

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52. The synthetic composition of claim 28 wherein the composition is a pharmaceutical composition.

5 53. A composition according to claim 28 wherein the composition is a vaccine.

54. A composition comprising an isolated antibody which binds to a conformational epitope of a protofibrillar aggregate which forms in a human or animal contributing to amyloid fibril formation.

10 55. A composition according to claim 54 wherein the antibody is effective to reduce the toxicity of the protofibrillar aggregate.

15 56. A composition according to claim 54 wherein the protofibrillar aggregate has a molecular weight in a range of about 1 kDa to about 100,000,000 kDa.

20 57. A composition according to claim 54 wherein the protofibrillar aggregate comprises five monomers.

58. A composition according to claim 54 wherein the protofibrillar aggregate comprises eight monomers.

25 59. A composition according to claim 54 wherein amyloid peptide monomers are substantially free of the conformational epitope.

60. A composition according to claim 54 wherein amyloid fibrils are substantially free of the epitope.

30 61. A composition according to claim 54 wherein the protofibrillar aggregate comprises a toxic species.

35 62. A composition according to claim 54 wherein the protofibrillar aggregate is present in a human or animal having a disease characterized by amyloid deposits.

63. A composition according to claim 62 wherein the disease is selected from the group consisting of Alzheimer's, early onset Alzheimer's associated with Down's syndrome, SAA amyloidosis, hereditary Icelandic syndrome, multiple myeloma, and spongiform encephalopathies, including mad cow disease, sheep scrapie, and mink spongiform encephalopathy, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, Creutzfeldt Jakob disease, Gerstmann-Straussler-Scheinker syndrome, kuru, fatal familial insomnia, chronic wasting syndrome, familial amyloid polyneuropathy, frontotemporal dementia, type II diabetes, systemic amyloidosis, serum amyloidosis, British familial dementia, Danish familial dementia, macular degeneration and cerebrovascular amyloidosis.

64. A composition according to claim 62 wherein the disease is Alzheimer's.

65. A composition according to claim 54 wherein the composition is a pharmaceutical composition.

66. A composition comprising an isolated antibody which binds to an epitope of a protofibrillar aggregate which forms in a human or animal contributing to an amyloid fibril formation wherein the amyloid fibril is substantially free of the epitope.

67. A composition according to claim in 66 wherein the protofibrillar aggregate comprises a toxic species.

68. A composition according to claim 66 wherein amyloid peptide monomers are substantially free of the epitope.

69. A composition according to claim 66 wherein the antibody is effective to reduce the toxicity of the protofibrillar aggregate.

70. A composition according to claim 66 wherein the protofibrillar aggregate has a molecular weight in a range of about 1 kDa to about 100,000,000 kDa.

71. A composition according to claim 66 wherein the protofibrillar aggregate comprises five monomers.

72. A composition according to claim 66 wherein the protofibrillar aggregate comprises eight monomers.

5 73. A composition according to claim 66 wherein the protofibrillar aggregate is present in a human or animal having a disease characterized by amyloid deposits.

10 74. A composition according to claim 73 wherein the disease is selected from the group consisting of Alzheimer's, early onset Alzheimer's associated with Down's syndrome, SAA amyloidosis, hereditary Icelandic syndrome, multiple myeloma, and spongiform encephalopathies, including mad cow disease, sheep scrapie, and mink spongiform encephalopathy, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, Creutzfeldt Jakob disease, Gerstmann-Straussler-Scheinker syndrome, kuru, fatal familial insomnia, chronic wasting syndrome, familial amyloid polyneuropathy, frontotemporal dementia, type II diabetes, systemic amyloidosis, serum amyloidosis, British familial dementia, Danish familial dementia, macular degeneration and cerebrovascular amyloidosis.

20 75. A composition according to claim 73 wherein the disease is Alzheimer's.

76. A composition according to claim 66 wherein the composition is a pharmaceutical composition.

25 77. A method of preventing or treating a disease or condition in a human or animal subject, the disease or condition being characterized by the presence of amyloid deposits comprising the step of:

30 A. administering to the subject a therapeutically effective or preventative amount of a composition comprising a conformational epitope of a protofibrillar aggregate which forms in a human or animal contributing to amyloid fibril formation.

78. A method according to claim 77 wherein step A comprises inducing an immune response against the conformational epitope.

35 79. A method according to claim 77 wherein the composition comprises a peptide component.

80. A method according to claim 79 wherein the peptide is conformationally constrained.

5 81. A method according to claim 79 wherein the peptide is selected from the group consisting of SEQ ID NO. 1, SEQ ID NO. 2, SEQ ID NO. 3, SEQ ID NO. 4, SEQ ID NO. 5, SEQ ID NO. 6, SEQ ID NO. 7, SEQ ID NO. 8, SEQ ID NO. 9 and mixtures thereof.

10 82. A method according to claim 79 wherein the peptide is SEQ ID NO. 1.

83. A method according to claim 77 wherein the composition is supported by a surface.

15 84. A method according to claim 83 wherein the surface is curved or flat.

85. A method of claim 83 wherein the surface comprises solid matter.

20 86. A method according to claim 83 wherein the surface is a film or a particle or a sheet.

87. A method according to claim 83 wherein the surface comprises a protein.

25 88. A method according to claim 86 wherein the protein comprises a -pleated sheet.

89. A method according to claim 83 wherein the composition is bound to the support surface.

30 90. A method according to claim 83 wherein the composition is chemically bonded to the support surface.

35 91. A method according to claim 90 wherein the chemical bond is a covalent bond.

92. A method according to claim 83 wherein the support comprises a material selected from the group consisting of gold, zinc, cadmium, tin, titanium, silver, selenium, gallium, indium, arsenic, silicon, mixtures thereof and combinations thereof.

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93. A method according to claim 77 wherein the protofibrillar aggregate has a molecular weight in a range of about 1 kDa to about 100,000,000 kDa.

94. A method according to claim 77 wherein the protofibrillar aggregate
10 comprises five monomers.

95. A method according to claim 77 wherein the protofibrillar aggregate comprises eight monomers.

15 96. A method according to claim 77 wherein amyloid peptide monomers are substantially free of the epitope.

97. A method according to claim 77 wherein amyloid fibrils are
20 substantially free of the epitope.

98. A method according to claim 77 wherein the protofibrillar aggregate comprises a toxic species.

25 99. A method according to claim 77 wherein the protofibrillar aggregate is present in a human or animal having a disease characterized by amyloid deposits.

100. A method according to claim 99 wherein the disease is selected from the group consisting of Alzheimer's, early onset Alzheimer's associated with
30 Down's syndrome, SAA amyloidosis, hereditary Icelandic syndrome, multiple myeloma, and spongiform encephalopathies, including mad cow disease, sheep scrapie, and mink spongiform encephalopathy, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, Creutzfeldt Jakob disease, Gerstmann-Straussler-Scheinker syndrome, kuru, fatal familial insomnia, chronic wasting
35 syndrome, familial amyloid polyneuropathy, frontotemporal dementia, type II diabetes, systemic amyloidosis, serum amyloidosis, British familial dementia, Danish familial dementia, macular degeneration and cerebrovascular amyloidosis.

101. A method according to claim 99 wherein the disease is Alzheimer's.

102. A method according to claim 77 wherein the composition is a vaccine.

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103. A method of preventing or treating a disease or condition characterized by amyloid deposits in a human or animal comprising the step of:

10 A. administering to the subject a therapeutically effective or preventative amount of a composition comprising an epitope of a protofibrillar aggregate which forms in a human or animal contributing to an amyloid fibril formation wherein the amyloid fibril is substantially free of the epitope.

104. A method according to claim 103 wherein step A comprises inducing an immune response against the conformational epitope.

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105. A method according to claim 103 wherein the amyloid peptide monomers are substantially free of the epitope.

20 106. A method according to claim 103 wherein the composition comprises a peptide component.

107. A method according to claim 106 wherein the peptide is conformationally constrained.

25 108. A method according to claim 106 wherein the peptide is selected from the group consisting of SEQ ID NO. 1, SEQ ID NO. 2, SEQ ID NO. 3, SEQ ID NO. 4, SEQ ID NO. 5, SEQ ID NO. 6, SEQ ID NO. 7, SEQ ID NO. 8, SEQ ID NO. 9 and mixtures thereof.

30 109. A method according to claim 106 wherein the peptide is SEQ ID NO. 1.

110. A method according to claim 103 wherein the composition is supported by a surface.

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111. A method according to claim 110 wherein the surface is curved or flat.

112. A method of claim 110 wherein the surface comprises solid matter.

113. A method according to claim 110 wherein the surface is a film or a particle or a sheet.

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114. A method according to claim 110 wherein the surface comprises a protein.

115. A method according to claim 114 wherein the protein comprises a -
10 pleated sheet.

116. A method according to claim 110 wherein the composition is bound to the support.

117. A method according to claim 110 wherein the composition is
15 chemically bonded to the support.

118. A method according to claim 117 wherein the chemical bond is a
20 covalent bond.

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119. A method according to claim 110 wherein the support comprises a material selected from the group consisting of gold, zinc, cadmium, tin, titanium, silver, selenium, gallium, indium, arsenic, silicon, mixtures thereof and combinations thereof.

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120. A method according to claim 103 wherein amyloid fibrils are substantially free of the epitope.

121. A method according to claim 103 wherein the protofibrillar aggregate
30 has a molecular weight in a range of about 1 kDa to about 100,000,000 kDa.

122. A method according to claim 103 wherein the protofibrillar aggregate comprises five monomers.

123. A method according to claim 103 wherein the protofibrillar aggregate
35 comprises eight monomers.

124. A method according to claim 103 wherein the protofibrillar aggregate comprises a toxic species.

125. A method according to claim 103 wherein the protofibrillar aggregate is present in a human or animal having a disease characterized by amyloid deposits.

126. A method according to claim 125 wherein the disease is selected from the group consisting of Alzheimer's, early onset Alzheimer's associated with Down's syndrome, SAA amyloidosis, hereditary Icelandic syndrome, multiple myeloma, and spongiform encephalopathies, including mad cow disease, sheep scrapie, and mink spongiform encephalopathy, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, Creutzfeldt Jakob disease, Gerstmann-Straussler-Scheinker syndrome, kuru, fatal familial insomnia, chronic wasting syndrome, familial amyloid polyneuropathy, frontotemporal dementia, type II diabetes, systemic amyloidosis, serum amyloidosis, British familial dementia, Danish familial dementia, macular degeneration and cerebrovascular amyloidosis.

127. A method according to claim 125 wherein the disease is Alzheimer's.

128. A method according to claim 103 wherein the composition is a vaccine.

129. A method of preventing or treating a disease or condition characterized by amyloid deposits in a human or animal subject comprising the step of:

A. causing an antibody to bind to a conformational epitope of a protofibrillar aggregate which forms in a human or animal contributing to fibril formation.

130. A method according to claim 129 wherein step A comprises administering to the subject a therapeutically effective or preventative amount of an antibody.

131. A method according to claim 129 wherein the protofibrillar aggregate comprises a toxic species.

132. A method according to claim 131 wherein the antibody is effective to reduce toxicity of the protofibrillar aggregate.

5 133. A method according to claim 129 wherein the protofibrillar aggregate has a molecular weight in a range of about 1 kDa to about 100,000,000 kDa.

134. A method according to claim 129 wherein the protofibrillar aggregate comprises five monomers.

10 135. A method according to claim 129 wherein the protofibrillar aggregate comprises eight monomers.

136. A method according to claim 129 wherein amyloid peptide monomers are substantially free of the epitope.

15 137. A method according to claim 129 wherein amyloid fibrils are substantially free of the epitope.

20 138. A method according to claim 129 wherein the protofibrillar aggregate is present in a human or animal having a disease characterized by amyloid deposits.

25 139. A method according to claim 138 wherein the disease is selected from the group consisting of Alzheimer's, early onset Alzheimer's associated with Down's syndrome, SAA amyloidosis, hereditary Icelandic syndrome, multiple myeloma, and spongiform encephalopathies, including mad cow disease, sheep scrapie, and mink spongiform encephalopathy, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, Creutzfeldt Jakob disease, Gerstmann-Straussler-Scheinker syndrome, kuru, fatal familial insomnia, chronic wasting syndrome, familial amyloid polyneuropathy, frontotemporal dementia, type II diabetes, systemic amyloidosis, serum amyloidosis, British familial dementia, Danish familial dementia, macular degeneration and cerebrovascular amyloidosis.

35 140. A method according to claim 138 wherein the disease is Alzheimer's.

141. A method according to claim 129 wherein the composition is administered by a method selected from the group consisting of intraspinal, intrathecal, oral, transdermal, pulmonary, intravenous, subcutaneous, intranasal, intraarterial, intracranial, intradermal, intraperitoneal, intramuscular, rectal and
5 buccal administration.

142. A method of preventing or treating a disease or condition characterized by amyloid deposits in a human or animal subject comprising the step of:
10 A . causing an isolated antibody to bind to an epitope of a protofibrillar aggregate which forms in a human or animal contributing to an amyloid fibril formation wherein the amyloid fibril is substantially free of the epitope.

143. A method according to claim 142 wherein step A comprises
15 administering to the subject a therapeutically effective or preventative amount of an antibody.

144. A method according to claim 142 wherein the protofibrillar aggregate has a molecular weight in a range of about 1 kDa to about 100,000,000 kDa.
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145. A method according to claim 142 wherein the protofibrillar aggregate comprises five monomers.

146. A method according to claim 142 wherein the protofibrillar aggregate
25 comprises eight monomers.

147. A method according to claim 142 wherein the protofibrillar aggregate comprises a toxic species.

148. A method according to claim 142 wherein the antibody is effective to
30 reduce toxicity of the protofibrillar aggregate.

149. A method according to claim 142 wherein amyloid fibrils are substantially free of the epitope.
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150. A method according to claim 142 wherein the protofibrillar aggregate comprises a toxic species.

151. A method according to claim 142 wherein the protofibrillar aggregate is present in a human or animal having a disease characterized by amyloid deposits.

5 152. A method according to claim 151 wherein the disease is selected from the group consisting of Alzheimer's, early onset Alzheimer's associated with Down's syndrome, SAA amyloidosis, hereditary Icelandic syndrome, multiple myeloma, and spongiform encephalopathies, including mad cow disease, sheep scrapie, and mink spongiform encephalopathy, Parkinson's disease, Huntington's
10 disease, amyotrophic lateral sclerosis, Creutzfeldt Jakob disease, Gerstmann-Straussler-Scheinker syndrome, kuru, fatal familial insomnia, chronic wasting syndrome, familial amyloid polyneuropathy, frontotemporal dementia, type II diabetes, systemic amyloidosis, serum amyloidosis, British familial dementia, Danish familial dementia, macular degeneration and cerebrovascular amyloidosis.

15 153. A method according to claim 151 wherein the disease is Alzheimer's.

20 154. A method according to claim 142 wherein the composition is administered by a method selected from the group consisting of intraspinal, intrathecal, oral, transdermal, pulmonary, intravenous, subcutaneous, intranasal, intraarterial, intracranial, intradermal, intraperitoneal, intramuscular, rectal and buccal administration.

25 155. A method of making an antibody comprising the step of:
A. obtaining a conformational epitope of a protofibrillar aggregate which forms in a human or animal contributing to amyloid fibril formation.

30 156. The method according to claim 155 wherein step A comprises recovering the antibody from a human or animal.

157. A method of making an antibody comprising the step of:
A. administering to a human or animal a composition comprising an
35 epitope of a protofibrillar aggregate which forms in a human or animal contributing to an amyloid fibril formation wherein the amyloid fibril is substantially free of the epitope.

158. The method according to claim 157 wherein step A comprises recovering the antibody from the human or animal.

5 159. A method of diagnosing a disease characterized by amyloid deposits comprising the step of:

A. combining tissue or fluid from a human or animal patient and a composition comprising an antibody which binds to a conformational epitope of a protofibrillar aggregate which forms in a human or animal contributing to amyloid fibril formation.

160. A method according to claim 159 wherein the disease is Alzheimer's disease.

15 161. A method according to claim 159 wherein the tissue or fluid is cerebrospinal fluid.

162. A method of diagnosing a disease characterized by amyloid deposits comprising the step of:

20 A. combining tissue or fluid from a human or animal patient and a composition comprising an antibody which binds to an epitope of a protofibrillar aggregate which forms in a human or animal contributing to an amyloid fibril formation wherein the amyloid fibril is substantially free of the epitope.

25 163. A method according to claim 162 wherein the disease is Alzheimer's disease.

164. A method according to claim 162 wherein the tissue or fluid is cerebrospinal fluid.

30 165. A method of assessing efficacy of a treatment method of a human or animal having a disease characterized by amyloid deposits comprising the steps of:

A. determining a baseline amount of an antibody specific for a conformational epitope of a protofibrillar aggregate which forms in a human or animal contributing to amyloid fibril formation in tissue sample from a patient before treatment with an agent and

B. comparing an amount of the antibody in the tissue sample from the subject after treatment with the agent to the baseline amount of the antibody.

5 166. A method according to claim 165 wherein a reduction or lack of significant difference between the amount of the antibody measured after the treatment compared to the baseline amount of the antibody indicates a negative treatment outcome.

10 167. A method according to claim 165 wherein a significantly greater amount of the antibody measured after the treatment compared to the baseline amount of the antibody indicates a positive treatment outcome.

15 168. A method according to claim 165, wherein the amounts of antibody are measured as antibody titers.

169. A method according to claim 165, wherein the amounts of antibody are measured by an ELISA assay.

20 170. A method of assessing efficacy of a treatment method of a human or animal having a disease characterized by amyloid deposits comprising the steps of:

25 A. determining a baseline amount of an antibody specific for an epitope of a protofibrillar aggregate which forms in a human or animal contributing to an amyloid fibril formation wherein the amyloid fibril is substantially free of the epitope in tissue sample from a patient before treatment with an agent

B. comparing an amount of the antibody in the tissue sample from the subject after treatment with the agent to the baseline amount of the antibody.

30 171. A method according to claim 170 wherein a reduction or lack of significant difference between the amount of the antibody measured after the treatment compared to the baseline amount of the antibody indicates a negative treatment outcome.

35 172. A method according to claim 170 wherein a significantly greater amount of the antibody measured after the treatment compared to the baseline amount of the antibody indicates a positive treatment outcome.

173. A method according to claim 170, wherein the amounts of antibody are measured as antibody titers.

5 174. A method according to claim 170, wherein the amounts of antibody are measured by an ELISA assay.

175. A diagnostic kit useful for detecting a disease characterized by amyloid deposits comprising:

10 a composition comprising an antibody which binds to a conformational epitope of a protofibrillar aggregate which forms in a human or animal contributing to amyloid fibril formation.

176. A diagnostic kit useful for detecting a disease characterized by amyloid deposits comprising:

15 an isolated composition comprising an antibody which binds to an epitope of a protofibrillar aggregate which forms in a human or animal contributing to an amyloid fibril formation wherein the amyloid fibril is substantially free of the epitope.

20 177. A method for assessing the ability of a test substance to inhibit the formation of amyloid oligomeric intermediates, said method comprising the steps of:

- A. preparing a first admixture containing the test substance and amyloid peptides;
- 25 B. incubating the first admixture under conditions where amyloid oligomeric intermediates would form from the amyloid peptides in the absence of any inhibitory effect;
- C. preparing a second admixture by combining the incubated admixture from Step B with antibodies that recognize conformational epitopes of the oligomeric intermediates; and
- 30 D. determining the amount of oligomeric intermediates formed on the basis of the binding of the antibody to conformational epitopes of the oligomeric intermediates.

35 178. A method according to Claim 177 wherein Step D is carried out by ELISA.

179. A method for assessing the ability of a test substance to cause the disassembly, disaggregation or substantial destruction of amyloid oligomeric intermediates, said method comprising the steps of:

- 5 A. preparing a first admixture containing amyloid oligomeric intermediates and the test substance; B. preparing a second admixture by combining the admixture from Step A with antibodies that recognize conformational epitopes of the oligomeric intermediates; and,
- 10 C. determining the amount of amyloid oligomeric intermediates that have not undergone disassembly, disaggregation or substantial destruction on the basis of the binding of the antibody to conformational epitopes of the oligomeric intermediates remaining in the second admixture.

- 15 180. A method according to Claim 178 wherein Step C is carried out by ELISA.